

**WHAT IS CLAIMED IS:**

1                   1.       A method of screening a candidate species for its ability to evoke a  
2 response in a target that produces a change in the environment of said target species, said  
3 method comprising:

4                   (a) forming a capsule containing said candidate species with said target and  
5 an intelligent substance which is defined as a substance that undergoes a  
6 transformation upon exposure to said change in environment, said candidate species  
7 and said target isolated from each other in said capsule and yet capable of being  
8 placed in contact by an externally imposed condition;

9                   (b) imposing said condition on said capsule, thereby placing said candidate  
10 species and said target in contact; and

11                  (c) monitoring said capsule for an indication of said transformation in said  
12 intelligent substance.

1                   2.       A method in accordance with claim 1 in which said target is a  
2 biological cell.

1                   3.       A method in accordance with claim 1 in which said target is an  
2 enzyme.

1                   4.       A method in accordance with claim 1 in which said target is a  
2 biological receptor.

1                   5.       A method in accordance with claim 4 in which said biological receptor  
2 is an intracellular receptor selected from the group consisting of estrogen receptors,  
3 glucocorticoid receptors, androgen receptors, progesterone receptors, and mineralocorticoid  
4 receptors.

1                   6.       A method in accordance with claim 1 in which said target is a  
2 transcription factor.

1                   7.       A method in accordance with claim 1 in which said target is a kinase.

1                   8.       A method in accordance with claim 1 in which said target is a member  
2 selected from the group consisting of proteins, sugars, nucleic acids, and lipids.

1                   9.       A method in accordance with claim 1 in which said target is an enzyme  
2 and said response is inhibition of said enzyme.

1                   10.      A method in accordance with claim 1 in which said target is a  
2 biological receptor and said response is activation of said receptor.

1                   11.      A method in accordance with claim 1 in which said target is a  
2 biological receptor and said response is an inhibition of the activation of said receptor due to  
3 competition for said receptor between said candidate species and a natural activator of said  
4 receptor.

1                   12.      A method in accordance with claim 1 in which said target is a  
2 biological cell and said response is agonist action on a receptor of said biological cell and a  
3 consequent intracellular process mediated by said agonist action.

1                   13.      A method in accordance with claim 1 in which said target is a  
2 biological cell and said response is antagonist action on a receptor of said biological cell and  
3 a consequent diminishment of an intracellular process due to said antagonist action.

1                   14.      A method in accordance with claim 1 in which said candidate species  
2 is a single molecular species.

1                   15.      A method in accordance with claim 1 in which said candidate species  
2 is a combination of molecular species.

1                   16.      A method in accordance with claim 1 in which said indication of said  
2 transformation in said intelligent substance is a member selected from the group consisting of  
3 a change in size of said capsule, a change in shape of said capsule, a change in an optical  
4 property of said intelligent substance, a release of a detectable species from said capsule, and  
5 an emission of a detectable signal from said capsule.

1                   17.      A method in accordance with claim 16 in which said indication of said  
2 transformation in said intelligent substance is a change in size of said capsule.

1                   18.      A method in accordance with claim 16 in which said indication of said  
2 transformation in said intelligent substance is a change in shape of said capsule.

1           **19.**     A method in accordance with claim **1** in which said intelligent  
2 substance is a crosslinked polymer and said change in environment is the release of an agent  
3 that disrupts the crosslinking in said polymer, thereby causing said polymer to swell.

1           **20.**     A method in accordance with claim **19** in which said polymer is  
2 crosslinked by antigen-antibody interaction between polymer chains to which antigen and  
3 antibody are covalently bound, and said change in environment is the release of free antigen  
4 or antibody that competes with said antigen-antibody interaction between polymer chains.

1           **21.**     A method in accordance with claim **19** in which said polymer is  
2 crosslinked by a linking group that is cleavable by an enzyme, and said change in  
3 environment is the release of said enzyme.

1           **22.**     A method in accordance with claim **21** in which said linking group is a  
2  $\beta$ -galactoside, and said change in environment is the release of  $\beta$ -galactosidase.

1           **23.**     A method in accordance with claim **16** in which said indication of said  
2 transformation in said intelligent substance is a change in fluorescence of said capsule.

1           **24.**     A method in accordance with claim **23** in which said change in  
2 fluorescence of said capsule is a fluorescence emission from an otherwise non-fluorescing  
3 capsule or an increase in fluorescence emission from said capsule.

1           **25.**     A method in accordance with claim **24** in which said intelligent  
2 substance comprises a support matrix with a fluorophore bound thereto, and said change in  
3 environment is the release of a cleaving agent that cleaves said fluorophore said support  
4 matrix, thereby causing a fluorescence emission.

1           **26.**     A method in accordance with claim **25** in which said fluorophore is a  
2 5-alkanoylamino fluorescein di- $\beta$ -galactopyranoside, and said cleaving agent is  $\beta$ -  
3 galactosidase.

1           **27.**     A method in accordance with claim **24** in which said intelligent  
2 substance comprises a crosslinked polymer with a fluorescence resonance energy transfer  
3 pair bound thereto and spaced apart to produce no net fluorescence, and said change in

environment is the release of an agent that disrupts the crosslinking in said polymer, thereby changing the spacing of said energy transfer pair and producing a net fluorescence.

28. A method in accordance with claim 1 in which said candidate species is a chemical compound.

29. A method in accordance with claim 28 in which said candidate compound is releasably immobilized on a solid support and said target is shielded from said solid support by a barrier that is impermeable to said solid support yet permeable to said candidate compound, and said externally imposed condition is a condition that causes release of said candidate compound from said solid support.

30. A method in accordance with claim 29 in which said solid support is a bead whose longest linear dimension is from about 1 nm to about 1 mm.

31. A method in accordance with claim 29 in which said solid support is a bead whose longest linear dimension is from about 0.5  $\mu\text{m}$  to about 500  $\mu\text{m}$ .

32. A method in accordance with claim 29 in which said candidate compound is covalently bonded to said solid support, and said externally imposed condition is a condition that causes cleavage of said candidate compound from said solid support.

33. A method in accordance with claim 32 in which said candidate compound is covalently bonded to said solid support through a nucleic acid linking group with a restriction site and step (b) comprises impregnating said capsule with a restriction enzyme effective to cause cleavage at said restriction site.

34. A method in accordance with claim 32 in which said candidate compound is covalently bonded to said solid support through a photocleavable linking group and step (b) comprises irradiating said capsule with light at a wavelength effective to cause cleavage of said linking group.

35. A method in accordance with claim 34 in which said photocleavable linking group is cleavable by ultraviolet light, said barrier shielding said biological cell from said solid support is a casing that is impermeable to ultraviolet light, and step (b) comprises irradiating said capsule with ultraviolet light.

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1           **36.**     A method in accordance with claim **1** in which step (a) comprises  
2     encasing said candidate species in a shell and forming said capsule around said shell with  
3     said target species external to said shell, and said externally imposed condition is a condition  
4     that renders said shell permeable to said candidate species.

1           **37.**     A method in accordance with claim **36** in which said shell is absorptive  
2     of electromagnetic radiation and rupturable by heat and step (b) comprises irradiating said  
3     shell with electromagnetic radiation.

1           **38.**     A method in accordance with claim **36** in which said shell encasing  
2     said candidate species is impermeable to said candidate species and is defined as a first shell  
3     and said target is surrounded by a second shell which is permeable to said candidate species  
4     and outside said first shell, said first shell being light absorptive and rupturable by heat and  
5     said second shell being transparent, and step (b) comprises irradiating said capsule with light  
6     thereby causing said first shell to rupture due to heat caused by light absorption without  
7     rupture of said second shell.

1           **39.**     A method in accordance with claim **36** in which said shell encasing  
2     said candidate species is impermeable to said candidate species and said target is embedded  
3     in a matrix that is outside said shell and permeable to said candidate species, and step (b)  
4     comprises rupturing said shell.

1           **40.**     A method in accordance with claim **36** further comprising encasing a  
2     plurality of magnetic particles in said shell with said candidate species, and step (b)  
3     comprises imposing a magnetic field on said capsule causing said magnetic particles to align  
4     and thereby rupture said shell.

1           **41.**     A method in accordance with claim **36** further comprising encasing a  
2     plurality of magnetic particles in said shell with said candidate species, and step (b)  
3     comprises imposing a magnetic field on said capsule to impart oscillating movement to said  
4     magnetic particles, said movement causing rupture of said shell.

1           **42.**     A method in accordance with claim **36** in which said shell comprises a  
2     material that is contractible upon exposure to an external stimulus, and step (b) comprises

3 exposing said shell to said external stimulus to cause contraction of said material sufficient to  
4 form channels through said shell for escape of said candidate species.

1           43.     A method in accordance with claim 36 further comprising encasing  
2 within said shell a solid particle which either contracts or expands upon exposing said shell to  
3 an external stimulus, and step (b) comprises exposing said shell to said external stimulus to  
4 cause sufficient contraction or expansion to rupture said shell.

1           44.     A method in accordance with claim 1 in which step (a) comprises  
2 sequestering said candidate species in a swollen hydrogen and forming said capsule around  
3 said hydrogel with said target external to said hydrogel, and said externally imposed  
4 condition is a condition that causes said hydrogel to contract and thereby expel said candidate  
5 species for contact with said target.

1           45.     A method of screening a plurality of candidate species for their ability  
2 to evoke a response in a target that produces a change in the environment of said target  
3 species, said method comprising:

4           (a) forming a plurality of capsules, each capsule containing one of said  
5 candidate species, a plurality of said target species, and an intelligent substance which  
6 is defined as a substance that undergoes a transformation upon exposure to said  
7 change in environment, said candidate species in each capsule isolated from said  
8 target in the same capsule and yet capable of being placed in contact with said target  
9 by an externally imposed condition;

10          (b) imposing said condition on said plurality of capsules, thereby placing said  
11 candidate species in contact with said target; and

12          (c) monitoring said capsules for an indication of said transformation in said  
13 polymer and identifying the candidate species contained in a capsule that exhibits said  
14 indication.

1           46.     A method in accordance with claim 45 in which each candidate species  
2 is a single molecular species.

1           47.     A method in accordance with claim 45 in which each candidate species  
2 is a combination of at least two distinct molecular species.

1           **48.**     A method in accordance with claim **45** in which said candidate species  
2 are chemical compounds that are releasably immobilized on microbeads with each candidate  
3 compound on a separate microbead and at most one microbead retained in each capsule, and  
4 said externally imposed condition is a condition that causes release of candidate compounds  
5 from all of said microbeads.

1           **49.**     A method in accordance with claim **45** in which said candidate species  
2 are chemical compounds that are releasably immobilized on microbeads on which are also  
3 immobilized identifier tags, each microbead having immobilized thereon a single candidate  
4 compound and a single identifier tag which comprises a detectable code that is decipherable  
5 to indicate the molecular structure of the candidate compound, and said externally imposed  
6 condition is a condition that causes release of all of said candidate compounds from said  
7 microbeads.

1           **50.**     A method in accordance with claim **45** in which said candidate species  
2 are peptides.

1           **51.**     A method in accordance with claim **49** in which said candidate species  
2 are peptides and each identifier tag is an oligonucleotide comprised of a sequence of codons  
3 corresponding to the sequence of amino acids in the peptide immobilized on the same  
4 microbead as said tag.

1           **52.**     A method in accordance with claim **49** in which said candidate species  
2 are chemical compounds and are immobilized on said microbeads in a manner that permits  
3 release of said chemical compounds without releasing said identifier tags.